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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,194	08/20/2008	Michael A. Caligiuri	22727/04450	5652

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EXAMINER	
KETTER, JAMES S	
ART UNIT	PAPER NUMBER
1636	

NOTIFICATION DATE	DELIVERY MODE
11/12/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/599,194	CALIGIURI ET AL.	
	Examiner	Art Unit	
	James S. Ketter	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 June 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/6/07; 1/20/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Group I, claims 1-12, in the reply filed on 30 august 2010 is acknowledged.

Claims 13-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 30 August 2010.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagashima et al. (cited as reference 11 on the IDS filed 6 August 2007).

Claim 1 is drawn to a method for stably transfecting mammalian primary natural killer cells comprising: transfecting a packaging cell line with a retroviral expression vector; culturing the transfected packaging cell line in a cell culture medium; and culturing the mammalian natural killer cells with the cell culture medium; wherein the transfected mammalian natural killer cells express an exogenous gene for at least two population doublings. Claim 5 specifies within claim 1 that comprising separating the transfected packaging cell line from the cell culture medium in which the cell line is cultured prior to culturing the mammalian natural killer cells with the cell culture medium.

Nagashima et al. teaches, e.g., at the Abstract, "Here, we demonstrate the successful delivery of the interleukin-2 (IL-2) gene into two human NK cell lines, IL-2-dependent NK-92 and IL-2-independent YT, by retroviral transduction. An MuLV-based retroviral vector expressing human IL-2 and neo^r markers from a polycistronic message was constructed and transduced into a CRIP packaging cell line. By coincubation of NK cells with monolayers of CRIP cells or by using retrovirus-containing supernatants in a flow-through method, 10% to 20% of NK cells were stably transduced. Upon selection in the presence of increasing G418 concentrations, transduced NK cells were able to proliferate independently of IL-2 for more than 5 months and to secrete up to 5.5 ng/10^6 cells/24 h of IL-2."

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagashima et al. (cited above) in view of Golay et al. (A, newly cited).

Claim 1 is described above, and is included in the rejection as it encompasses the limitations of the dependent claims. Claim 2 specifies within claim 1 that the packaging cell line is chosen from a Phoenix cell line. Claim 3 specifies within claim 2 that the packaging cell line is Phoenix-Ampho. Claim 4 specifies within claim 1 that the retroviral expression vector is

PINCO. Claim 6 specifies within claim 1 that the transfected mammalian natural killer cells include both CD56(bright) and CD56(dim) cell subsets.

Nagashima et al. is described above. Nagashima et al. differs from the claimed invention in not teaching the Phoenix or Phoenix-Ampho cell line or the PINCO retroviral expression vector. Golay et al. teaches, e.g., at paragraphs [0029]-[0033], the use of PINCO retroviral vector and Phoenix-Ampho cells for transfection with the exogenous gene. The substitution of one known element (the PINCO expression vector and the Phoenix-Ampho cell line of Golay et al.) for another (MuLV and CRIP of Nagashima et al.) would have been obvious to one of ordinary skill in the art at the time of the invention since the substitution of the vector and cell line of Golay et al. would have yielded predictable results, namely, packaging and transduction of a vector containing the gene of interest of Nagashima et al.

Claims 1 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagashima et al. (cited above) in view of Fischer et al. (U, newly cited).

Claim 1 is described above, and is included in the rejection as it encompasses the limitations of the dependent claims. Claim 7 specifies within claim 1 that the vector comprises cDNA of greater than about 2 kB. Claim 8 specifies within claim 7 that the vector comprises cDNA of greater than about 3 kB. Claim 9 specifies within claim 8 that the vector comprises cDNA of greater than or equal to about 3.8 kB. Claim 10 specifies within claim 9 that the vector comprises cDNA of greater than about 4 kB.

Nagashima et al. is described above. Nagashima et al. differs from the claimed invention in not teaching the recited sizes of the cDNA insert. Fischer et al. is cited to show that inserts up

to 6 or 7 kB were known to be useable in retroviral vectors. The substitution of one known element (inserts of any length up to 6 or 7 kB as shown to be known in the art by Fischer et al.) for another (the insert of unspecified size taught by Nagashima et al.) would have been obvious to one of ordinary skill in the art at the time of the invention since the insertion of any DNA of interest up to 6 or 7 kB into a retroviral vector would have yielded predictable results, namely, packaging and transduction of a vector containing any gene of interest, the vector and cells shown by Nagashima et al.

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagashima et al. (cited above) in view of Campana et al. (B, newly cited).

Claim 11 is drawn to a non-naturally occurring mammalian CD56dim natural killer cell which expresses an exogenous protein of interest and at least one of green fluorescent protein and CD8. Claim 12 is drawn to a progeny cell line of the non-naturally occurring mammalian natural killer cell according to claim 11.

Nagashima et al. is described above. Nagashima et al. differs from the claimed invention in not teaching GFP marker from the vector. Campana et al. teaches, e.g., at paragraph [0125], the use of GFP as a marker in a retroviral vector, itself used in NK cells. Thus, it would have been recognized by one of ordinary skill in the art that applying the known technique taught by Camapana et al. to the vector, and thus cells, of Nagashima et al. would have yielded predicable results and resulted in an improved system, namely, a system that would express a marker gene in the system of Nagashima et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James S. Ketter whose telephone number is 571-272-0770. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSK
8 November 2010

/James S. Ketter/
Primary Examiner, Art Unit 1636